

Amendments to the Specification:

Please replace the Summary of the Invention paragraph that begins on page 5, line 8 with the following replacement paragraph:

It is an object of the present invention to provide methods and compositions for targeting nucleic acids to cells and to particular cellular compartments of eukaryotic cells, especially the mitochondria. The compositions of the present invention are peptide-nucleic acid complexes, in which the peptide and nucleic acid are covalently joined, including linkage via a third "linker" component. It is the peptide portion of the complex which directs the nucleic acid to the cellular compartment of interest. It is preferred that the nucleic acid be such that it can be incorporated as a ~~relicative~~ replicative nucleic acid, and it should have properties which result in controlled transcription and/or replication in cells and in defined targeted (aimed) compartments. Specifically exemplified peptide sequences are given in SEQ ~~IDS~~ ID NO:1 and SEQ ID NO:22.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-83 (canceled).

84. (Currently amended) A chimeric peptide-nucleic acid construct comprising:
- (a) a mitochondria-specific signal peptide, wherein the peptide does not comprise a KDEL signal sequence, and wherein the peptide has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:22,
  - (b) a linkage agent covalently linked to an amino acid at the carboxy-terminal end of the signal peptide, and
  - (c) a linear nucleic acid, wherein said nucleic acid is covalently linked to the linkage agent,
- whereby the signal peptide is linked to the nucleic acid via the linkage agent in the construct so that the chimeric peptide-nucleic acid construct enters mitochondria.
85. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the nucleic acid has secondary structure.
86. (Previously presented) The chimeric peptide-nucleic acid construct of claim 85, wherein the nucleic acid comprises a partially palindromic sequence.
87. (Canceled)
88. (Previously presented) The chimeric peptide-nucleic acid construct according to claim 84, wherein phosphodiester bonds of the nucleic acid are substituted with phosphorus thioate bonds.

89. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the nucleic acid comprises a reactive linkage group.
90. (Previously presented) The chimeric peptide-nucleic acid construct of claim 89, wherein the reactive linkage group contains an amino function and the linkage agent contains an amino-reactive group.
91. (Previously presented) The chimeric peptide-nucleic acid construct of claim 89, wherein the reactive linkage group contains a thiol function and the linkage agent contains a thiol-reactive group.
92. (Previously presented) The chimeric peptide-nucleic acid construct of claim 89, wherein the linkage group is bound to the nucleic acid via a spacer comprising at least two carbon atoms.
93. (Previously presented) The chimeric peptide-nucleic acid construct of claim 92 wherein the linkage group present is bound to the nucleic acid via a spacer comprising six carbon atoms.
94. (Currently amended) The chimeric peptide-nucleic acid construct of claim 90, wherein the linkage group is ~~localized~~ located at the 3' ~~hydroxy/phosphate~~ hydroxy or 3' phosphate terminus or at the 5' ~~hydroxy/phosphate~~ hydroxy or 5' phosphate terminus of the linear nucleic acid.
95. (Previously presented) The chimerical peptide-nucleic acid construct of claim 94, wherein an additional nucleic acid, an antisense oligonucleotide, a messenger RNAs or a transcribable and/or replicative gene is covalently linked with the 5' terminus and/or 3' terminus of the nucleic acid.
96. (Currently amended) The chimeric peptide-nucleic acid construct of claim 95, further comprising a promoter, wherein the promoter is a mitochondrial promoter.

97. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the signal peptide has a reactive amino acid at the carboxy-terminal end and wherein the linkage agent contains an amino-reactive or thiol-reactive group.
98. (Previously presented) The chimeric peptide-nucleic acid construct of claim 97, wherein the reactive amino acid at the carboxyl-terminal end is lysine or cysteine.
99. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the signal peptide comprises a mitochondria-specific peptidase cleavage site.
100. (Previously presented) The chimeric peptide-nucleic acid construct of claim 99, wherein the peptide consists of the mitochondria-specific cleavable signal peptide of human mitochondrial ornithine transcarbamylase, extended by an cysteine at the C terminus.
101. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent is a bifunctional or a heterobifunctional cross-linker.
102. (Currently amended) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent contains thiol-reactive and/or amino-reactive groupings function when the signal peptide and the nucleic acid carry thiol and/or amino groups as linkage sites.
103. (Currently amended) The chimeric peptide-nucleic acid construct of claim 84, wherein the linkage agent is m-maleimido-benzoyl-N-hydroxy-succinimide ester ~~or a derivative thereof~~.

104. (Previously presented) The chimeric peptide-nucleic acid construct of claim 84, wherein the molecule penetrates mitochondrial membranes by utilizing natural transport mechanisms.
105. (Currently amended) A chimeric peptide-nucleic acid construct, wherein the peptide has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:22, of a linear-cyclic nucleic acid molecule, wherein the molecule comprises at least one replication origin and wherein both ends of the molecule are cyclized, said cyclized plasmid having at least one cyclic end having a modified nucleotide which via a linkage agent is linked with a mitochondria-specific or membrane-specific signal peptide.
106. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the nucleic acid portion further comprises at least one promoter.
107. (Previously presented) The chimeric peptide-nucleic acid construct of claim 106, wherein at least one promoter is a mitochondrial promoter.
108. (Previously presented) The chimeric peptide-nucleic acid construct of claim 107, wherein the mitochondrial promoter is the mitochondrial promoter of the light strand.
109. (Previously presented) The chimeric peptide-nucleic acid construct of claim 106, wherein the molecule comprises further mitochondrial transcription-regulatory sequences.
110. (Previously presented) The chimeric peptide-nucleic acid construct of claim 109, wherein the transcription-regulatory sequences are 3' of the promoter.

111. (Previously presented) The chimeric peptide-nucleic acid construct of claim 109, wherein the transcription-regulatory sequences comprise elements of the mitochondrial H-strand and L-strand transcription control elements.
112. (Previously presented) The chimeric peptide-nucleic acid construct of claim 111, wherein said L-strand transcription control elements are conserved-sequence-blocks.
113. (Previously presented) The chimeric peptide-nucleic acid construct of claim 108, wherein the transcription-regulatory sequences comprise a binding sequence of a mitochondrial transcription termination factor.
114. (Previously presented) The chimeric peptide-nucleic acid construct of claim 113, wherein the transcription termination factor is a bidirectionally acting transcription termination factor.
115. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the replication origin is a mitochondrial replication origin.
116. (Previously presented) The chimeric peptide-nucleic acid construct of claim 115, wherein the replication origin is the replication origin of the heavy mtDNA strand and comprises at least one 'conserved sequence block'.
117. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the plasmid nucleic acid portion further comprises a selection gene.
118. (Previously presented) The chimeric peptide-nucleic acid construct of claim 117, wherein the selection gene is an antibiotic-resistance gene.

119. (Previously presented) The chimeric peptide-nucleic acid construct of claim 118, wherein the antibiotic-resistance gene is an oligomycin-resistance gene or a chloramphenicol-resistance gene.
120. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the molecule further comprises a multiple cloning site.
121. (Previously presented) The chimeric peptide-nucleic acid construct of claim 120, wherein the multiple cloning site comprises recognition sequences for restriction endonucleases which do not occur in another site of the plasmid.
122. (Previously presented) The chimeric peptide-nucleic acid construct of claim 121, wherein the multiple cloning site is arranged in the 3' direction of the promoter and in the 5' direction of the transcription termination site.
123. (Previously presented) The chimeric peptide-nucleic acid construct of claim 121, wherein the multiple cloning site is arranged in the 5' direction of the selection gene.
124. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the ends of the nucleic acid are covalently joined to the peptide.
125. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the linear-cyclic plasmid nucleic acid portion has 5' overhangs which do not have a palindromic sequence and which sequences are not complementary to one another.
126. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein the ends of the nucleic acid construct are cyclized via synthetic oligonucleotides.

127. (Previously presented) The chimeric peptide-nucleic acid construct of claim 105, wherein a restriction endonuclease is to generate overhanging ends in the linear-cyclic plasmid nucleic acid portion of the construct.
128. (Previously presented) The chimeric peptide-nucleic acid construct of claim 127, wherein the restriction endonuclease is Bsal.
129. (Currently amended) A method for the production of a chimeric peptide-nucleic acid construct which enters mitochondria, said method comprising the steps of:
- (a) reacting a nucleic acid or oligonucleotide containing a functional linkage group having a linkage agent to form a construct,
  - (b) reacting of the construct of (a) with amino acids at the carboxy-terminal end of a peptide containing a signal sequence, wherein the signal sequence is not a KDEL signal sequence, and wherein the peptide has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:22, to form a chimeric peptide-nucleic acid linked construct; and
  - (c) optionally extending the chimeric peptide-nucleic acid linked construct of step (b) by binding or covalently joining a further nucleic acid molecule.
130. (Previously presented) The method of claim 129, wherein the further nucleic acid molecule in step (c) comprises a human mitochondrial promoter of light strand (P<sub>L</sub>) and a mitochondrial transfer RNA leucine (tRNA<sup>LeuUUR</sup>) gene.
131. (Previously presented) A method for introducing the chimeric peptide-nucleic acid construct of claim 105 into cells or mitochondria, said method comprising contacting the chimeric peptide-nucleic acid construct with cells or mitochondria.



132. (Previously presented) The method of claim 131, wherein the mitochondria are energized mitochondria.
133. (Previously presented) The method of claim 131, wherein the cells are eukaryotic cells.
134. (Previously presented) The method of claim 131, wherein the contacting is via a particle gun system, electroporation, microinjection or lipotransfection.